DISSERTATION ON

CUTANEOUS TUBERCULOSIS - INCIDENCE AND CLINICOHISTOPATHOLOGICAL CORRELATON

This dissertation is submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the requirement of the award
for the degree of

M.D BRANCH XX

DERMATOLOGY, VENEREOLOGY AND LEPROSY

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DECLARATION

I solemnly declare that the dissertation titled **CUTANEOUS TUBERCULOSIS – INCIDENCE AND CLINICOHISTOPATHOLOGICAL CORRELATION** was done by me at Department of Dermatology, Stanley Medical College and Hospital during 2008-2011 under the guidance and supervision of my **Chief Prof Dr. K.Manoharan, M.D.,D.D.**

This dissertation is submitted to **THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY** towards partial fulfillment of requirement for the award of **M.D.Degree(Branch XII) in DERMATOLOGY, VENEREOLOGY AND LEPROSY.**

Place :

Date :

DR.S.ATHILAKSHMI

CERTIFICATE

This is to certify that this dissertation titled **'CUTANEOUS TUBERCULOSIS - INCIDENCE AND CLINICO HISTOPATHOLOGICAL CORRELATION'** is submitted by **Dr.S.ATHILAKSHMI** to **The Tamilnadu Dr. M.G.R. Medical university, Chennai** in partial fulfillment of requirement of the award for the degree of **M.D BRANCH XX (DERMATOLOGY, VENEREOLOGY AND LEPROSY)** and is a bonafide work done by her under direct supervision and guidance.

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CONTENTS

INTRODUCTION

Tuberculosis, one of the oldest diseases known to mankind, continues to be a major public health problem in the world today , especially in developing countries like India. According to WHO, over one third population are at risk in developing tuberculosis today. Extrapulmonary TB constitutes only 10% of all cases of tuberculosis and cutaneous TB accounts to about 1.5% of all such cases. Improved living standards, effective screening and treatment have greatly reduced the prevalence of TB in industrialised countries but resurgence is being witnessed in developing countries.

The factors responsible for resurgence are

- overcrowding due to migration of infected people from areas of high prevalence to low endemic areas
- worsening urban economic and social environment
- emergence of MDR M.tuberculosis
- increasing incidence of AIDS

Though cutaneous TB constitutes only a minor proportion , bearing in mind the prevalence of TB, these numbers become significant. Cutaneous TB can mimic the clinicopathological features of many other skin diseases, and underlying systemic or organ TB can be difficult to detect, resulting in diagnostic challenges and pitfalls and potential delays in diagnosis and institution of treatment.

The varied clinicopathological features of cutaneous TB are attributed to

- pathogenecity of organism
- resistance of the organism
- portal of infection
- immune status of the host

Cutaneous manifestations of TB include a wide and often overlapping spectrum of papules, pustules, papulonecrotic , nodular, verrucous lesions, panniculitis, plaques, ulcers, sinuses, scars.

This study was undertaken to unravel the variations in morphology and clinicohistopathological correlation of various types of cutaneous TB.

AIM OF THE STUDY

To find out the incidence of various morphological types and clinicohistopathological correlation of cutaneous TB presenting to our department and to compare that in the literature.

REVIEW OF LITERATURE

Just as systemic TB can be protean and diverse in its clinical manifestations, so tuberculosis of the skin is also highly variable in its clinical appearance, significance, and prognosis.

Bacteriology

The causative bacterium is Mycobacterium tuberculosis ,discovered by Robert koch in 1882[3]. It measures 2.5 to 3.5 μm in length by 0.3 to 0.6μm in width.

This slightly curved ,sporeless,motile,obligate aerobic gram positive bacterium is acid and alcohol fast.

The cell wall of the mycobacterium contain mycolic acid which protects bacterium from cell lysosomal attack. Lipoarabinomannon is present in the plasma membrane.

There are two types of M. TB involved in cutaneous TB – human (common) and bovine (rare).

Epidemiology

Cutaneous tuberculosis forms a small proportion of extra pulmonary TB. The incidence of cutaneous TB has fallen from 2% to 0.15% in India. But in the present scenario, the disease is fast reappearing due to HIV pandemic and emerging MDR M.tuberculosis.

Disease transmission

In pulmonary TB transmission is mainly by inhalation of airborne droplets and rarely by direct inoculation. the mode of infection in cutaneous TB may be exogenous (eg) autoinoculation, or endogenous (eg) extension of an underlying diseased organ or by lymphatic or haematogenous spread[1].

PATHOGENESIS AND IMMUNOLOGY

Various factors involved in the pathogenesis are

Infection and invasion:

The interaction of M.tuberculosis with the human host begins when droplet nuclei containing micro organisms from infectious patients are inhaled.

Virulence of tubercle bacilli[4]:

Several genes are responsible for the virulence of the bacilli like

- kat gene which encodes for catalase enzyme that protect against oxidative stress
- rpo V gene is the main factor initiating transcription of several genes
- erp gene encodes a protein required for multiplication

Innate resistance to infection:

Polymorphisms in multiple genes, such as those encoding for HLA, TGF- ß, IL-10, Mannose binding protein, Toll like receptor 2, IL-2 have been associated with susceptibility to tuberculosis. Several genetic factors play a key role in innate nonimmune response to infection with M. tuberculosis. The NRAMP1 gene, which maps to chromosome 2q, may play a role in determining susceptibility to tuberculosis.

Granuloma formation:

With the development of specific immunity and the accumulation of large numbers of activated macrophages at the site of primary lesion, tubercles are formed. It consists of accumulation of lymphocytes and activated macrophages that evolve toward epitheloid and giant cell morphologies.

Role of monocytes and macrophages:

Cell mediated immunity confers partial protection against M. tuberculosis. Monocytes and macrophages , attracted to the site , are the key components of immune response. These cells produce nitric oxide and cytokines, which has anti mycobacterial activity.

Role of T lymphocytes:

Activated CD4+ T lymhocytes differentiate in to cytokine producing Th 1 or Th 2 cells.

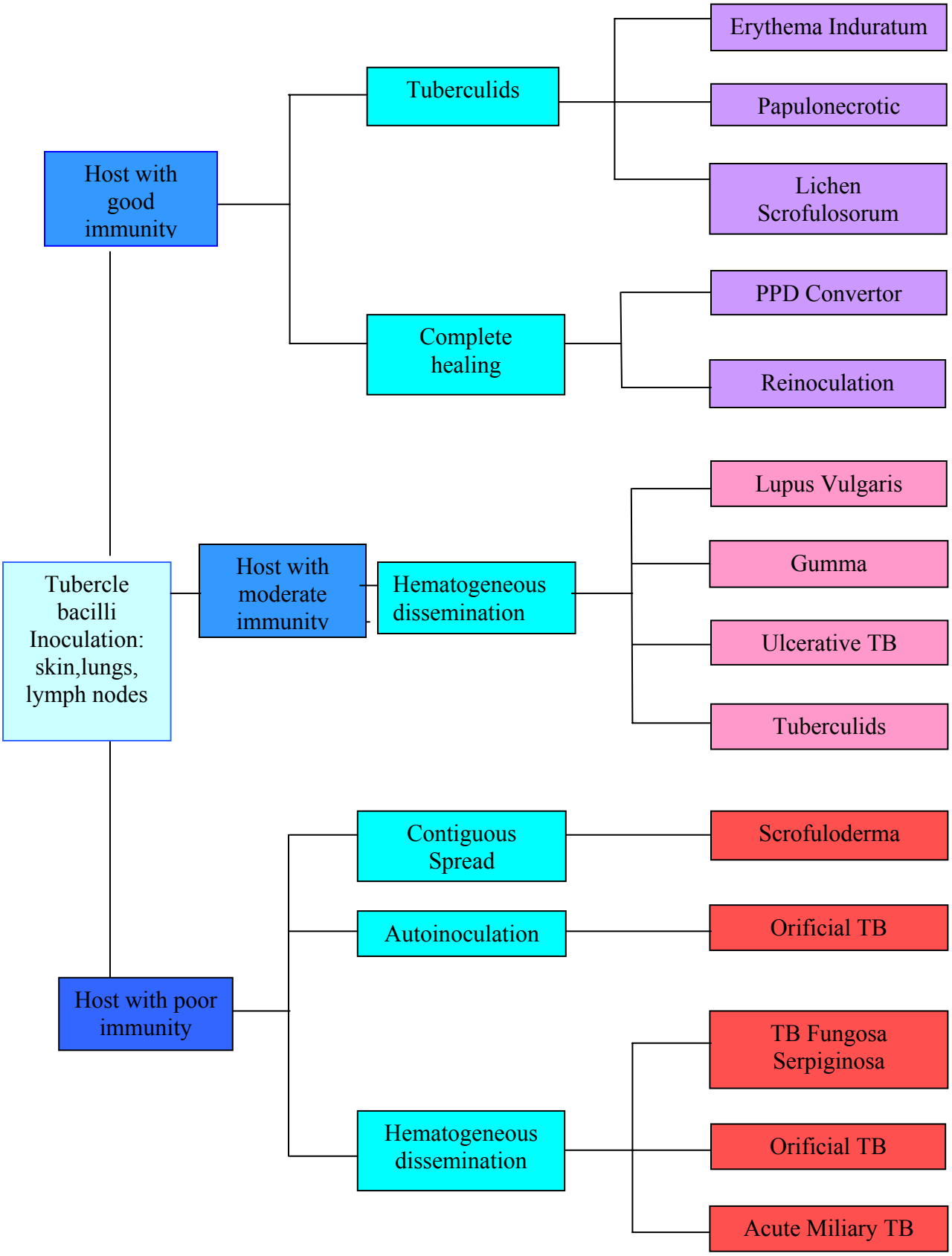
Th1 cells produce IFN γ, which is activator of monocytes and macrophages.

Th2 cells produce IL-4, IL-5, IL-10, IL-13. These cytokines promote intracellular killing of mycobacteria.

Mycobacterial lipids and proteins:

Lipids have been involved in mycobacterial recognition by innate immune system, and lipoproteins have been proven to trigger potent signals through TLRs , present in blood dendritic cells. M. tuberculosis possesses various protein antigens, which are important in eliciting a T lymphocyte response. Among the antigens that may play a protective role are the 30kDa and ESAT-6 antigens.

Schematic representation of pathogenesis of Cutaneous TB



CLASSIFICATION

The most widely accepted classification for cutaneous TB is based on the mechanism of disease propogation as proposed by Beyt et al in 1981[6].

1)Exogenous source	- Tuberculous chancre
	- warty tuberculosis
	- Lupus vulgaris (some)
2)Endogenous source	
Contiguous spread	- Scrofuloderma
Autoinoculation	- Orificial tuberculosis
3) Hematogenous	- Miliary tuberculosis
	- Lupus vulgaris
	- Tuberculous gumma
4)Eruptive tuberculosis (tuberculids)	
Micropapular	- Lichen scrofulosorum
Papular	- Papulonecrotic tuberculid
Nodular	- Erythema induratum of Bazin , Erythema nodosum

An additional classification system was designed based on bacterial load. This system is extremely similar to Ridley and Jopling's description of M.leprae in Hansen's disease[2].

1) Multi bacillary form which contains abundant bacilli

- Tuberculous chancre
- Tuberculous Gumma
- Acute miliary tuberculosis
- Periorificial tuberculosis
- Scrofuloderma

2) Pauci bacillary form

- Warty TB
- Lupus vulgaris

TUBERCULOUS CHANCRE

Synonynm: primary inoculation tuberculosis

Definition:

Tuberculous chancre develops as a result of inoculation of M.tuberculosis in to the skin of an individual without any immunity to the organism.

Pathogenesis:

The inoculation occurs on the exposed areas, especially extremities and face, from cuts, abrasions, scratches, circumcision, ear piercing, tattooing, mouth to mouth respiration[10].

Clinical features :

After an incubation period of about 3-4 weeks following inoculation, a papule develops, which quickly breaks down to form an indolent ,firm, ragged ulcer with undermined edge and granular haemorrhagic base. Later it becomes firm and thin adherent crust develops[11]. Sometimes the initial lesion is small and characteristic apple-jelly nodules may be demonstrated.[5] Three types of lesions have been described[1] – chancriform type, impetigenous type and echthymatous type.The chancriform lesion has a classic regional lymphadenopathy that occurs about 3-4 weeks after the development of the ulcer. This may be seen with or without an

intervening lymhangitis, which may be tender and have cord-like induration. This primary complex has great diagnostic value.Inoculation about the nail may produce painless paronychia[12]. conjunctival edema and irritation have been described. Oral lesions are uncommon.

Tuberculin test:

Tuberculin test negative early in the course of disease.

Histopathology:

Aute neutrophilic reaction with areas of necrosis, ulceration and numerous bacilli present. After 3-6 weeks, due to development of immunity, the infiltrate becomes granulomatous. Epitheloid cells, Langhans giant cells and peripheral rim of lymphocytes are present.

Course and prognosis:

The chancre will heal slowly, taking many months, but may rarely proceed to lupus vulgaris. Erythema nodosum may occur in 10% cases[13]. In patients with poor immunity and high bacterial load, acute military tuberculosis can develop.

Differential diagnosis:

In the early ulcerative phase, the diseases to be considered are the ulcerative pyodermas, atypical mycobacterial infections, chancre, cutaneous leishmaniasis ,cutaneous malignancies with local metastasis.

WARTY TUBERCULOSIS

Synonyms: Tuberculosis verrucosa cutis

Prosector's wart

Verruca necrogenica

Post primary inoculation tuberculosis

Verrucous tuberculosis

Anatomist's wart

Definition:

It is an indolent, warty, plaque-like form of tuberculosis occurring as a result of inoculation of the organism in to the skin of a previously infected patient with moderate or high degree of immunity.

Pathogenesis:

- Accidental infection in phycicians, pathologists, lab workers, postmortem attendants[14]
- Autoinoculation with sputum in individuals with active tuberculosis
- Children and young adults with moderate immunity,who come in contact with infected Material[15]

Clinical features:

Lesions occur most on those areas exposed to trauma and to infected sputum or oter tuberculous material. Commonly affected sites are the knees, ankles, buttocks[16]. The initial lesion is a painless, dusky- red papule that expands peripherally and is surrounded by an inflammatory halo. Irregular extension at the edges leads to serpiginous outline with finger-like projections. The centre may involute producing an atrophic scar. The consistency is firm and a probe cannot be passed.Beads of pus may be expressed from softer areas. Lymphadenopathy is characteristically rare or absent.

Unusual variants[17] are

- Psoriasiform
- Keloidal
- Exudative
- Ulcerative

- Granulomatous
- Crusted
- Deeply destructive papillomatous
- Sclerotic forms.

Tuberculin test:

Tuberculin test is usually positive.

Histopathology:

Epidermis shows hyperkeratosis, acanthosis, papillomatosis, pseudoepitheliomatous hyperplasia.Upper dermis shows abscess formation and tuberculoid granulomas with a slight to moderate amount of caseation necrosis are present in the mid dermis.

Course and prognosis:

Spontaneous involution can occur over months to years resulting in atrophic scar[18].Overall,the prognosis is good.

Differntial diagnosis:

Subungual and digital verruca, atypical mycobacterial infections, hypertrophic lichen planus, blastomycosis, chromoblastomycosis,tertiary syphilis, leishmaniasis.

SCROFULODERMA

S**ynonym:** Tuberculosis colliquativa cutis

Definition:

It results from involvement and breakdown of the skin overlying a contiguous tuberculous focus which is usually a lymph gland, infected bone or joint, lacrimal gland or duct[19].

Pathogenesis:

It usually extends from underlying infected lymph node, but also may present as an extension of disease from an underlying infected joint, tendon, bursa, bone, or tuberculous epididymitis. In children, the infection is mainly due to bovine tubercle bacillus as a result of tonsillar infection.

Clinical features:

The initial lesion is a firm, subcutaneous or deep cutaneous nodule which later ulcerates. The ulcer has a bluish undermined edge with granulating tissue at the base. Fistulae and sinuses may be formed beneath ridges of a bluish skin. Multiple lesions may be produced following haematogenous dissemination. Cervical nodes are most commonly affected followed by axillary, inguinal, epitrohlear, retro auricular nodes[20]. it is the commonest form of cutaneous tuberculosis in Indian children[21]. As a result of progression and scarring,

irregular cicatricial bands may be produced. Fungating tumours may develop due to excessive granulation tissue and secondary bacterial infections. After healing, characteristic puckered scarring occur[23].

Tuberculin test :

Strongly positive

Histopathology:

Epidermis shows ulceration and necrosis.Dermis shows an ulcerated abscess with marked caseation necrosis. Numerous bacteria can be demonstrated.

Course and prognosis:

Spontaneous healing can occur, but the course is very protracted and leaves typical cord-like structures. Lupus vulgaris can develop from the scar of scrofuloderma. Malignant change in the form of epithelioma can occur.

Differential diagnosis:

Atypical mycobacterial infections, tularemia, lymphopathia venerum, actinomycosis, nocardiosis, hidradenitis suppurativa, syphilitic gumma, acne conglobata.

ORIFICIAL TUBERCULOSIS

Synonyms: Acute tuberculous ulcer

Tuberculosis cutis orificialis

Definition:

Tuberculous infection of mucous membrane and skin of orifices, resulting from auto inoculation of the tubercle bacilli in patients with advanced visceral tuberculosis.

Pathogenesis:

This is normally a form of autoinoculation tuberculosis, although extraneous sources are occasionally responsible[24]. the lesions occur in advanced pulmonary, intestinal or genitourinary disease.

Clinical features:

Ulcerative lesions occur in the oral cavity, perianal and perirectal areas. The tip and lateral margins of the tongue are most commonly involved. The initial lesion is a small, yellowish or reddish nodule that rapidly breaks down to form an exquisitely painful, shallow ulcer with bluish, undermined edges.

Tuberculin test:

Usually anergy present due to lowered immunity.

Histopathology:

Non specific. Inflammatory infiltrate with pronounced necrosis present in lower dermis. Numerous bacilli can be demonstrated.

Course and prognosis:

No tendency for spontaneous healing and has a poor prognosis.

Differential diagnosis:

Syphilitic chancre, luetic gumma, aphthosis, deep mycosis, granulomatous vasculitis, local or metastatic malignancy.

LUPUS VULGARIS

Synonym – Tuberculosis cutis luposa

Definition:

A chronic progressive post primary form form of cutaneous tuberculosis in an individual with moderate or high degree of immunity.

Pathogenesis:

It can arise by contiguous, lymphatic or hematogenous spread. It may develop at the site of tuberculous chancre, in the scar of scrofuloderma, BCG vaccination scar[25].

Clinical features:

The initial lesion is a small, reddish- brown, flat plaque of soft, almost gelatinous consistency. On diascopy, the characteristic apple jelly nodules can be demonstrated. The lesion extends peripherally with central atrophy or scarring. The reactivation of nodules within previously atrophic or scarred areas is characteristic. Multiple lesions are uncommon. Probe can be easily passed as it is soft in consistency.Females are more commonly affected than males. In India, face is affected less commonly and buttocks and trunk more frequently[26]. Mucosal involvement involving nasal, buccal or conjunctival mucosa can occur.

Clinical variants:

- plaque type with psoriasiform scaling
- ulcerative and mutilating type- scarring and ulceration predominate. Crusts form over areas of necrosis. Contractures and deformities can develop.
- vegetating form or lupus vegetans or lupus papillomatosus- characterized by marked infiltration, ulceration and necrosis. Mucous membrane and cartilage are involved resulting in extensive destruction.
- lupus vulgaris verrucosus
- lupus vulgaris involving mucous membrane or lupus vorax
- lupus postexathematicus- due to lowered immunity following a viral exanthem

- tumour-like form- presents as hypertrophic or myxomatous forms which may cause lymphedema and vascular dilatation.
- papular and nodular forms- multiple lesions occur in disseminated lupus- true military lupus
- sporotrichoid form

Tuberclin test:

Usually positive.

Histopathology:

Epidermis is normal or ulcerated or atrophic or acanthotic with pseudoepitheliomatous hyperplasia.Upper dermis shows well formed granulomas, composed of epitheloid cells, Langhan giant cells and lymphocytes. Caseation necrosis is absent or minimal. Bacilli usually not found.

Course and prognosis:

Lupus vulgaris can be a very protean, destructive disease. It progresses slowly over years, without treatment. Severe scarring, disfigurement and mutilation can occur. Long standing cases can be complicated by squamous cell carcinoma, basal cell carcinoma,sarcoma. Hodgkin's disease.

Differential diagnosis:

Leishmaniasis, sarcoidosis, facial granulomas, erythema elevatum diutinum, leprosy, psoriasis,

Bowen's disease, halogenodermas, blastomycosis, lupus pernio, rhinoscleroma.

MILIARY TUBERCULOSIS

Synonyms: Haematogenous primary tuberculosis

Miliaris disseminatus

Definition:

It occur in association with generalized military tuberculosis and is due to haematogenous dissemination of mycobacteria into skin.

Pathogenesis:

It is rare and usually occur and usually occur in young children or immunosuppressed patients[27].

Clinical features:

The primary lesions are discrete, pinhead-sized, bluish- red macules or papules or vesicles, which soon burst and form crusts. Ulcerations, subcutaneous nodules, purpuric

lesions can also occur.

Tuberculin test:

Always negative.

Histopathology:

Focal areas of necrosis and abscess formation containing numerous bacilli.

Course and prognosis:

Poor prognosis and death is due to overwhelming infection.

TUBERCULOUS GUMMA

Synonym: Metastatic tuberculous abscess

Definition:

It result from hematogenous dissemination from primary focus during periods of lowered resistance, resulting in single or multiple lesions. It is seen in malnourished children,after local trauma and in association with underlying lymphoma.

Clinical features:

Presents as a firm , subcutaneous nodule in extremities. Later it forms abscess, which breaks down to form an undermined ulcer with sinuses. Lesions may occur in

sporotrichoid fashion.

Tuberculin test:

Modest sensitivity.

Differential diagnosis:

Syphilitic gumma, subcutaneous bacterial, mycotic lesions, panniculitides

RARE FORMS OF CUTANEOUS TUBERCULOSIS

Tuberculosis fungosa serpiginosa:

It is a very rare chronic form ofskin tuberculosis, which occurs in anergic,elderly individuals via exogenous or endogenous inoculation. Patients present with thick, papillomatous, vegetative, noncornified plaques, commonly in the axilla and dorsum of hands.Numerous bacilli can be found in the lesions. Tuberculin test is negative.

Iatrogenic immunization tuberculosis:

Lupus vulgaris,scrofuloderma,acute military tuberculosis can develop following BCG vaccination. Since BCG organism is an attenuated M.tuberculosis bovis, it can behave as a virulent opportunistic pathogen whenever immunity is suppressed.

Tuberculous mastitis:

Patients present with nontender cold abscess in the breast.

TUBERCULIDS

A tuberculid is a cutaneous immunological reaction to the presence of occult TB in a patient with moderate to high immunity.

The main features of tuberculids as first described by Jean Darier in 1896[28],are

- positive tuberculin skin test
- tuberculous involvement of lymph nodes,viscera or both
- absence of tubercle bacilli in the lesion
- skin lesions that heal on remission of the tuberculous infection.

LICHEN SCROFULOSORUM

Synonym: Tuberculosis cutis lichenoides

Definition and pathogenesis:

First described by Hebra. It is a lichenoid eruption occurring in children and adolescents. Its onset may be linked to an up-regulation in immune status[30].

Clinical features:

The eruption is characterized by asymptomatic, pin-head sized, lichenoid or skin coloured, follicular or perifollicular papules. Common sites are abdomen, chest, back and proximal limbs.

Tuberculin test:

Always positive.

Histopathology:

Superficial dermal granulomas around hair follicles and sweat ducts. Epitheloid cells, lymphocytes and occasional giant cells are seen.

Course and prognosis:

Spontaneous resolution can occur but recurrences are possible.

Differential Diagnosis:

Lichenoid id, secondary eruptions of treponemal infections, lichen nitidus, eruptive syringoma, and a drug eruption.

PAPULONECROTIC TUBERCULID

Synonym: tuberculosis cutis papulonecrotica

Definition and pathogenesis:

It is an eruption of necrotizing papules affecting the extensor aspect of extremities and is associated with deep focus of tuberculosis.

Clinical features;

The eruption consists of recurring crops of symmetrical, hard,dusky-red papules. These crust, ulcerate, leaving atrophic, varioliform scars[31]. Young adults are affected. Most common sites are legs, knees, elbows, buttocks, penis.

Tuberculin test:

Strongly positive.

Histopathology:

Leukocytoclastic vasculitis is present in early cases. Later, wedge-shaped necrosis develops. Epitheloid cells and giant cells are seen at the periphery of necrotic zone. Blood vessel involvement is a key feature.

Course and prognosis;

Disease may last for years or decades with recurrent crops of ulceration and consequent varioliform scarring.

Differential Diagnosis:

Pityriasis lichenoides, leukocytoclastic vasculitis, nodular prurigo.

ERYTHEMA INDURATUM OF BAZIN

Synonym: Bazin's disease

Tuberculosum

Tuberculosis cutis indurativa

Nodose tuberculid

Definition and pathogenesis:

It is characterized by inflammatory cutaneous and subcutaneous nodules in an individual with past or active tuberculosis. It is believed to be an allergic or hypersensitivity reaction to tubercle bacilli[32].

Clinical features:

Symmetrical, tender, firm, well circumscribed nodules. Lesions may ulcerate following cold exposure. The ulcers are ragged, irregular, shallow with a bluish edge. Typically affects the calves of pubertal or adult women[33].

Tuberculin test:

Strongly positive.

Histopathology:

Early stage - inflammation of vessel wall with lymphocytic and plasma cell infiltrate

with thickening of adventitia and media. Perivascular infiltrate is present.

- A septal panniculitis is present, which may overflow in to the fat lobules.
- A lobular granulomatous reaction develops which may lead to atrophy of fat tissues[34,35].

Late stage - caseation and liquefaction develop and fibrosis occur.

Course:

May wax and wane for many years. Good prognosis is expected if no general disease is found.

ERYTHEMA NODOSUM

Definition and pathogenesis:

It is an acute, nodular, erythematous eruption that is usually limited to the extensor aspects of the lower legs, with occasional spread to thighs or arms. It is presumed to be a hypersensitivity reaction and may occur in association with tuberculosis[36].

Other triggering factors

1) sarcoidosis

2) inflammatory bowel disease

3) infections

4) drug therapies

5) idiopathic in 70% of cases.

Clinical features:

It is the most common panniculitis in India. Erythema nodosum may occur in children and patients older than 70 years, but it is more common in young adults aged 18-34 years. As a manifestation of tuberculosis, erythema nodosum has been described in children with primary tuberculosis infection and may be associated with phlyctenular conjunctivitis. Low grade fever and swelling of the ankle joints accompany the skin lesions in some patients. Immune complex deposition within dermal vessels is an important component in the production of the symptom complex. Patients usually present with skin rash in the form of dusky red, tender and nodular lesions. Lesion borders are poorly defined and size vary from 2-6 cm. Individual lesions last approximately two weeks, but occasionally, new lesions continue to appear for three to six weeks. Arthralgia occurs in more than 50% of patients and begins during the eruptive phase or precedes the eruption by 2-4 weeks. Any joint may be involved, but the ankles, knees, and wrists are affected most commonly. No destructive joint changes occur. Synovial fluid is acellular, and the rheumatoid factor is negative. When erythema nodosum is diagnosed, it is important to find out the underlying conditions.

Tuberculin test:

The tuberculin skin test is always strongly positive and a negative skin test rules out tuberculosis as the etiology.

Histopathology:

Histopathologically, erythema nodosum is the stereotypical example of a mostly septal panniculitis with no vasculitis[6]. The septa of subcutaneous fat are always thickened and variously infiltrated by inflammatory cells that extend to the periseptal areas of the fat lobules. Usually, a superficial and deep perivascular inflammatory infiltrate predominantly composed of lymphocytes is also seen in the overlying dermis. This dermal inflammation along with vasodilatation probably accounts for the erythematous appearance of early lesions, whereas the changes in the subcutis are responsible for the nodularity of the lesions on palpation. A histopathologic hallmark of erythema nodosum is the presence of the so-called Miescher's radial granulomas[6], that consist of small, well-defined nodular aggregations of small histiocytes around a central stellate or banana shaped cleft . In early lesions, Miescher's radial granulomas appear scattered in the septa and surrounded by neutrophils. In older nodules of erythema nodosum, histiocytes coalesce to form multinucleated giant cells, many of which still retain in their cytoplasm a stellate central cleft reminiscent of those centers of Miescher's radial granuloma . Miescher's radial granulomas are present in all stages of the evolution of erythema nodosum lesions and they should be searched for in order to make a specific diagnosis.

Course and prognosis:

Erythema nodosum tends to disappear by itself and often does not need any specific treatment. Generally, the prognosis of erythema nodosum is very good.

CRITERIA FOR DIAGNOSIS OF CUTANEOUS TUBERCULOSIS

Major criteria:

- Culture for AFB positive
- Positive animal inoculation
- PCR positive

Minor critera:

- Compatible histopathology
- AFB in the lesion
- Positive tuberculin test
- Active visceral tuberculosis
- Raised ESR
- Response to 6 weeks of trial with anti tuberculous therapy

DIAGNOSIS

A clinical diagnosis of cutaneous tuberculosis can be made confidently in most instances but requires confirmation by any of the following investigations.

CULTURE METHODS[3]

Can be either solid or liquid media

Solid media

Lowenstein-jensen medium is the most well known medium

Specimen may be inoculated in to the medium and incubated at 37°c. growth detected after4-8 weeks.

Liquid media

A number of commercial liquid-based mycobacterial culture systems include BACTEC 460 TB system , BACTEC Mycobacterial Growth Indicator Tube 960 system.

The medium contains radiolabelled palmitic acid as a sourceof carbon and this is metabolized by the growing organisms. The amount of carbondioxide emitted is monitered by repeated aspiration of the atmosphere in each vial to detect its growth. Growth can be detected in 10-22 days and the recovery rate is 88%-100%.

Identification from culture is by performing Ziehl-Neelson staining or auromine-rhodamine staining.

Other methods like

1) niacin test

2) mycolic acid analysis by high-performance liquid chromatography ,

3) genotype assays

can also be employed for detection of mycobacterium in culture.

PCR[37]

Polymerized chain reaction DNA amplification by PCR is another rapid, sensitive method that has been used to detect cutaneous TB in several studies, most commonly targeting the IS6110 gene specific for the M.tuberculosis complex. However, PCR is a labor-intensive technique and is susceptible to several technical errors. It may provide false-positive results by carry-over contamination. False-negative results may be caused by degraded target DNA, the presence of PCR-inhibiting substances in clinical samples or insufficient extraction of target DNA. Moreover, it cannot be used to test drug susceptibility. Finally, the high cost of this technique becomes prohibitive for its use, especially in a resource-poor country like India.

HISTOPATHOLOGY[39]

The hallmark of cutaneous tuberculosis is the presence of tuberculous or tuberculoid granuloma.

Seven patterns have been described:

1) Classic tuberculoid granulomas, which consist of typical granulomas with Langhans giant cells. A peripheral cuff of lymphocytes surrounds the giant cells. Caseation necrosis may or may not be present.

2) Abscess formation,which consists of acute or chronic inflammatory cells with variable degree of necrosis. Giant cells are seen only in few cases.

3) Diffuse infiltration of histiocytes with few other inflammatory cells. Only a few well formed granulomas are seen. Necrosis is universal.

4) Panniculitis involving both seta and lobules. Abscess formation and necrosis can occur. Phlebitis can be found rarely.

5) Nonspecific chronic inflammation, which includes sheets or scattered clusters of chronic inflammatory cells consisting predominantly of lymphocytes and histiocytes. Plasma cells and eosinophils can also be seen. Giant cells are absent.

6) Sarcoidal granulomas - naked granulomas. Consist mainly Langhans giant cells, no peripheral rim of lymphocytes. Necrosis is minimal or absent. Lamellar calcifications identical to Schaumann bodies are sometimes present.

7) Rheumatoid nodules, the hallmark of which is the presence of central necrosis surrounded by palisading histiocytes, in the dermis or subcutis.

MYCO DOT TEST[41]

Mycobacteria are known to have several immunologically active antigenic components like 38 Kd antigen, 30 Kd antigen, 16 Kd antigen, A60 antigen and lipoarabinomannan (LAM). The MycoDot test is a new simple, rapid (20 minutes) and reliable serodiagnostic technique that can detect anti-mycobacterial antibodies in the serum or blood. It offers a low cost, single visit aid in the diagnosis of tuberculosis, with good sensitivity and excellent specificity .

The MycoDot test employs lipoarabinomannan (LAM) antigen which is bound to plastic combs. When the combs are incubated in diluted serum/blood, specific anti-LAM antibodies from the sample, if present, bind to the antigen. The sensitivity of the test is calibrated so that only cases of active mycobacterial diseases such as tuberculosis will generate a colored spot, which is as strong as or stronger than the weakest positive spot on the reference comb that is provided as a guide to interpret results. Healthy infected and/or BCG vaccinated individuals react negatively.

IMMUNE-BASED TESTS[5]

I)Tuberculin sensitivity test or Mantoux test[3]

History:

Tuberculin is a glycerol extract of the tubercle bacillus. Purified protein derivative (PPD) tuberculin is a precipitate of non-species-specific molecules obtained from filtrates of sterilized, concentrated cultures. It was first described by Robert Koch in 1890. The test is named after Charles Mantoux, a French physician who developed on the work of Koch and Clemens von Pirquet to create his test in 1907.

Procedure

The suitable dilution of standard dose of tuberculin (standard dose 5TU) is injected in the inner aspect of forearm. A weal of 5mm should be raised. The reaction is read after 48 to 72 hours. The induration is measure not the redness (erythema) surrounding it.

Dosage of tuberculin

The dose is 0.1ml.

In 0.1 ml of diluent contains 0.0001mg of Purified protein derivative (PPD) which is equivalent to 5Tuberculin units (TU).

PPD is obtained by culturing Mycobacterium tuberculosis H37RA strain with TWEEN 80 on a protein free medium Quinsol.

If a person has had a history of a positive tuberculin skin test, or has not had a recent tuberculin skin test (within one year), another skin test may be needed; if negative.

Interpretation of tuberculin reaction

The results of this test must be interpreted carefully. The person's medical risk factors determine at which increment (5 mm, 10 mm, or 15 mm) of induration the result is considered positive. A positive result indicates TB exposure.

- 5 mm or more is positive in
  - HIV-positive person
  - Recent contacts of TB case
  - Persons with nodular or fibrotic changes on chest x-ray consistent with old healed TB
  - Patients with organ transplants and other immunosuppressed patients
- 10 mm or more is positive in
  - Recent arrivals (less than 5 years) from high-prevalence countries
  - Injection drug users
  - Residents and employees of high-risk congregate settings (e.g., prisons, nursing homes, hospitals, homeless shelters, etc.)
  - Persons with clinical conditions that place them at high risk
  - Children less than 4 years of age, or children and adolescents exposed to adults in high-risk categories

- 15 mm or more is positive in

  - Persons with no known risk factors for TB

  A tuberculin test conversion is defined as an increase of 10 mm or more within a 2-year period, regardless of age.

False positive result

Due to the test's low specificity, most positive reactions in low-risk individuals are false-positives. A false positive result may be caused by nontuberculous mycobacteria or previous administration of BCG vaccine.
Prior vaccination with BCG may result in a false-positive result for many years afterwards.
False positives can also occur when person touches the injected area, causing swelling and itching.

False negative result

Those that are immunologically compromised, especially those with HIV and low CD4 T cell counts, frequently show negative results from the PPD test. This is because the immune system needs to be functional to mount a response to the protein derivative injected under the skin.

Anergy testing

In cases of anergy, a lack of reaction by the body's defence mechanisms when it comes into contact with foreign substances, the tuberculin reaction will occur weakly, thus compromising the value of Mantoux testing. For example, anergy is present in AIDS, a disease which strongly depresses the immune system. Therefore, anergy testing is advised in cases where suspicion is warranted that it is present. However, routine anergy skin testing is not recommended.

II)Interferon-gamma release assays (IGRA)[4]

Used in the diagnosis of latent TB infection.

Antigens used:

1) Early secreted antigenic target 6 (ESAT-6)
2) Culture filtrate protein 10 (CFP-10)
3) TB7.7

Commercially available IGRAs

1) Quanti-FERON TB Gold assay
2) T-SPOT test

QUANTI-FERON-TB GOLD IN-TUBE[42] (QFT-IT)

This in vitro interferon-gamma-release assay is useful in the diagnosis of tubercular infection. It is considered to be superior to tuberculin skin testing owing to its higher specificity. In fact, in a rural and predominantly BCG-vaccinated pediatric population in India, the tubercular skin test and QFT-IT assay were found to produce comparable results in the diagnosis of tubercular infection without any obvious advantage of the latter.

ANTITUBERCULAR DRUG TRIAL[43] (THERAPEUTIC TRIAL)

The concept of therapeutic challenge as a valid diagnostic method in doubtful cases of cutaneous TB (where laboratory results are equivocal) has been corroborated in adults, and can be extended to the pediatric population as well. Four-drug antitubercular (ATT) therapy (consisting of isoniazid, rifampicin, pyrazinamide and ethambutol) is initiated and the clinical response is assessed in 4-6 weeks. If there is no significant response by 5 weeks, it is unlikely that further treatment may be beneficial. In such a case, either the diagnosis should be reviewed or possibility of MDR TB should be considered. However, patients with tuberculids and those with minimally active disease may take longer than 5 weeks to respond, and thus it may be worthwhile to prolong the therapeutic trial in such cases before considering alternative diagnoses.

TREATMENT

Cutaneous TB is treated as per the recommendations of therapy for extrapulmonary TB[44] (category 3).

Apart from the investigations to establish the diagnosis of cutaneous TB, HIV testing should be carried out in all patients with confirmed or suspected TB because their HIV status makes a difference to their antitubercular treatment.

Classification of anti tubercular drugs:

First line drugs:

1) Ethambutol - EMB or E,
2) Isoniazid - INH or H,
3) Pyrazinamide - PZA or Z,
4) Rifampicin -RMP or R,
5) Streptomycin - STM or S.

Second line drugs:

There are six classes of second-line drugs (SLDs) used for the treatment of TB. A drug may be classed as second-line instead of first-line for one of three possible reasons: it may be less effective than the first-line drugs (e.g., p-aminosalicylic acid); or, it may have toxic side-effects (e.g., cycloserine)

1) Aminoglycosides: e.g., amikacin (AMK), kanamycin (KM);

2) Polypeptides: e.g., capreomycin, viomycin, enviomycin;

3) Fluoroquinolones: e.g., ciprofloxacin (CIP), levofloxacin, moxifloxacin (MXF);

4) Thioamides: e.g. ethionamide, prothionamide

5) Cycloserine (the only antibiotic in its class);

6) p-Aminosalicylic acid (PAS or P).

Third line drugs:

Other drugs that may be useful are

1) Rifabutin

2) Macrolides: e.g., clarithromycin (CLR);

3) Linezolid (LZD);

4) Thioacetazone (T);

5) Thioridazine;

6) Arginine;

7) Vitamin D;

Standardized Treatment Regimens are one of the pillars of the DOTS strategy

Isoniazid, Rifampicin, Pyrazinamide, Ethambutol, and Streptomycin are the primary antitubercular drugs used. Most DOTS regimens have thrice-weekly schedules and typically last for 6 months, with an initial Intensive phase and a Continuation phase.Based on the nature/severity of the disease and the Patients' exposure to previous anti-tubercular treatments,

RNTCP classifies tuberculosis patients in to three Treatment Categories[37].

Category I	Category II	Category III
New sputum smear-positive Seriously ill sputum smear-negative Seriously ill extra-pulmonary New Sputum Positive/Negative HIV Positive	Sputum smear-positive Relapse Sputum smear-positive Failure Sputum smear-positive Treatment after default Sputum smear negative Others/Chronic	New sputum smear-negative, not seriously ill New extra-pulmonary, not seriously ill
$2H_3R_3Z_3E_3 + 4H_3R_3$	$2H_3R_3Z_3E_3S_3 + 1H_3R_3Z_3E_3 + 5H_3R_3E_3$	$2H_3R_3Z_3 + 4H_3R_3$
2 months Intensive phase + 4 months continuation phase Four drugs at Thrice-weekly Schedule	3 months Intensive phase + 5 months continuation phase Five drugs at Thrice-weekly Schedule	2 months Intensive phase + 4 months continuation phase Two drugs at Thrice-weekly Schedule

H: Isoniazid (600 mg), R: Rifampicin (450 mg), Z: Pyrazinamide (1500 mg),

E: Ethambutol (1200 mg), S: Streptomycin (750 mg)

PREVENTION

BCG vaccination[45]

Bacillus Calmette-Guérin (or Bacille Calmette-Guérin, BCG) is a vaccine against tuberculosis that is prepared from a strain of the attenuated (weakened) live bovine tuberculosis bacillus, Mycobacterium bovis that has lost its virulence in humans by being specially cultured in an artificial medium for years. The bacilli have retained enough strong antigenicity to become a somewhat effective vaccine for the prevention of human tuberculosis. At best, the BCG vaccine is 80% effective in preventing tuberculosis for a duration of 15 years.

Description:

BCG Vaccine is a live freeze-dried vaccine derived from attenuated strain of mycobacterium bovis. (Bacillus Calmette Gueri) used for the prevention of tuberculosis.

Composition:

Live, attenuated BCG Vaccine (Bacillus Calmette Gueri strain)

Each 0.1 ml contains between: $1x10^5$ and $33x10^5$ C.F.U.

Reconstitute with Sodium Chloride Injection

Dosage and administration:

The vaccine is intended to be injected strictly via the intradermal route, avoiding the subcutaneous route.The vaccination dose is 0.05 ml for children under one year of age including the new born, of the reconstituted vaccine given intrademally. The skin should not be cleaned with antiseptic. The vaccine should be preferably given with a tuberculin syringe or 25G/26G sterile needle and syringe.Skin testing with tuberculin is not generally carried out before giving BCG, but when performed, those who are found to be positive reactors need not to be immunised.

Indications and immunization schedule:

BCG Vaccine should be given routinely to all infants at risk of early exposure to tuberculosis. This vaccine should be given soon after the child is born. BCG administered early in life provides high level of protection particularly against sever forms of childhood tuberculosis and tubercular meningitis. In countries with low prevalence of tuberculosis, BCG vaccination should be restricted to high-risk groups such as hospital personnel and tuberculin negative contacts of known cases of tuberculosis. The vaccine can be given simultaneously with DTP, DT, TT, Measles, Polio and Hepatitis B vaccines, but at a separate site.

Adverse effects:

Adverse events occur in 1-10% of individuals who receive BCG and vary depending upon dosage, method of administration and age of vaccine[46]. Lymphadenitis can also occur.

- Lymphangitis can occur if the vaccine is administered too close to the shoulder and is characterized by streaking from site of injection towards the regional lymph nodes.
- Lymphadenopathy of regional lymph nodes, which resolves spontaneously, occurs occasionally in young children.
- Osteomyelitis has been reported to occur rarely (one case per million vaccines) and most frequently in neonates.
- Disseminated BCG infection, which can be fatal, occurs rarely in 1-10 cases per 10 million vaccines and is more common in immunodeficient children.

Skin Complications:

Local

- Keloid
- Large ulcer
- Subcutaneous abscess
- Epithelial cyst
- Granulomatous reaction
- Lupus vulgaris
- Warty TB

Generalized

- Erythema nodosum
- Tuberculids
- Scrofuloderma
- Nonspecific haemorrhagic eruption

MATERIALS AND METHODS

Background

Resurgence of tuberculosis in the era of HIV has rejuvenated the interest in this global problem. Moreover there is increased incidence of tuberculosis, due to multidrug resistant strains of M.tuberculosis. Transmission of cutaneous tuberculosis is facilitated by overcrowding, malnutrition and low socio economic status. Though the incidence of Cutaneous tuberculosis is low worldwide it is increasing in developing countries like India.

This study is undertaken to unravel the variations in morphology and histopathology of Cutaneous tuberculosis and create awareness about Cutaneous tuberculosis.

Study Design:

Prospective Study

Study Procedure:

Patients attending Dermatology OPD,Govt Stanley hospitals with clinical suspicion of cutaneous tuberculosis, who are histopathologically proven , will be included in this study.

Study Duration:

One Year-May 2009 to April 2010

INVESTIGATIONS

Patients included in this study wer subjected to the following investigations\

- Total count
- Differential count
- ESR
- Haemoglobin%
- Mantoux test
- Sputum for AFB
- Chest X-ray
- Skin biopsy
- Elisa for HIV
- Screening forVDRL

RESULTS

Out of 30 cases studied, males were found to be more commonly affected than females.There were 16 males, 12 females and 2 male children. Depending upon morphological features and histopathological features, 30 cases were typified and of this

14 cases had warty tuberculosis,

9 cases had lupus vulgaris,

2 cases had scrofuloderma

2 cases had papulonecrotic tuberculid

2 cases had erythema nodosum and

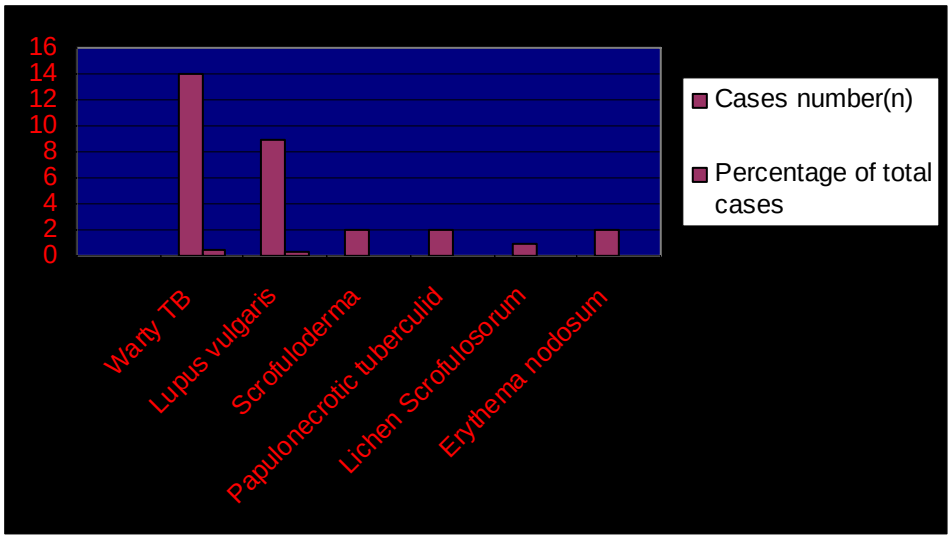
1 was a case of lichen scrofulosorum.

Histopathological correlation was present in all cases except a case of scrofuloderma, which showed only ulceration of the epidermis and few lymphocytic infiltrate in the dermis. Patients with warty TB showed characteristic tuberculoid granulomas(11 cases) in the mid dermis and epidermal changes were present in 10 cases. Out of 9 cases of lupus vulgaris epidermal changes were present in 4 cases, characteristic tuberculoid granulomas was present in 3 cases, Langhans giant cells were present in 4 cases. Ziehl-Neelson stain was performed on all cases but could demonstrate AFB only in one case of scrofuloderma. AFB culture was done in 2 cases of scrofuloderma and the result was negative in both cases.

Chest x-ray finding consistent with tuberculosis was present in 10 cases. Of this hilar adenitis was present in 3 cases, apical opacity was present in 2 cases. Mantoux was present in all cases except one case of scrofuloderma, which may be due to anergy.

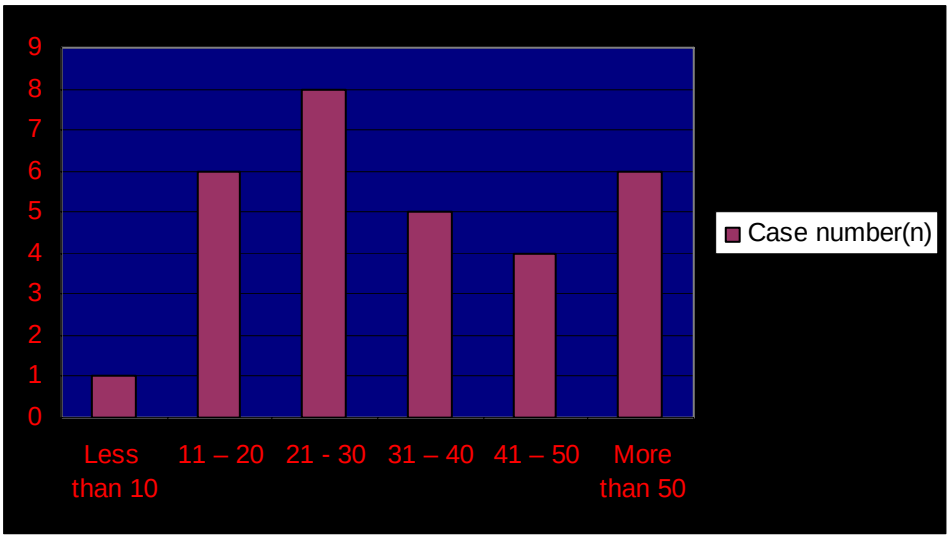
The highest age incidence was found to be between 20 – 30 years and most of the patients with cutaneous TB, who were included in the study were males. Of the 30 cases studied, lymphadenopathy was present in 3 cases- tender matted lymphadenitis was present in 1 case of scrofuloderma and a case of warty TB over right knee joint and non tender ipsilateral cervical lymphadenopathy was present in 1 case of lupus vulgaris involving right forearm.

INCIDENCE AND PERCENTAGE OF VARIOUS MORPHOLOGICAL TYPES OF CUTANEOUS TB



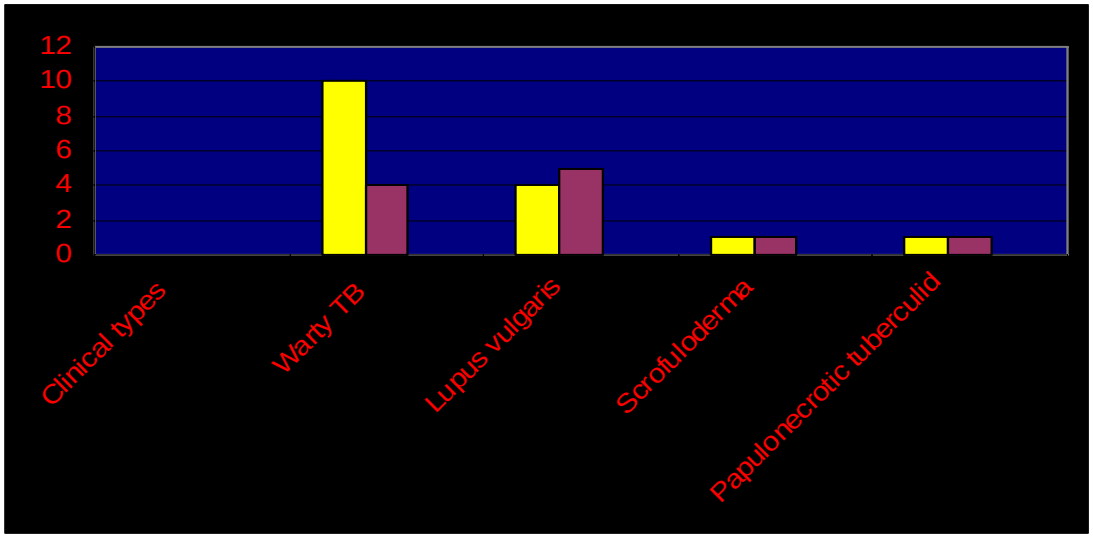
Clinical types	Cases number(n) total cases - 30	Percentage of total cases
Warty TB	14	46.66
Lupus vulgaris	9	30
Scrofuloderma	2	6.66
Papulonecrotic tuberculid	2	6.66
Lichen Scrofulosorum	1	3.33
Erythema nodosum	2	6.66

AGE DISTRIBUTION OF CASES



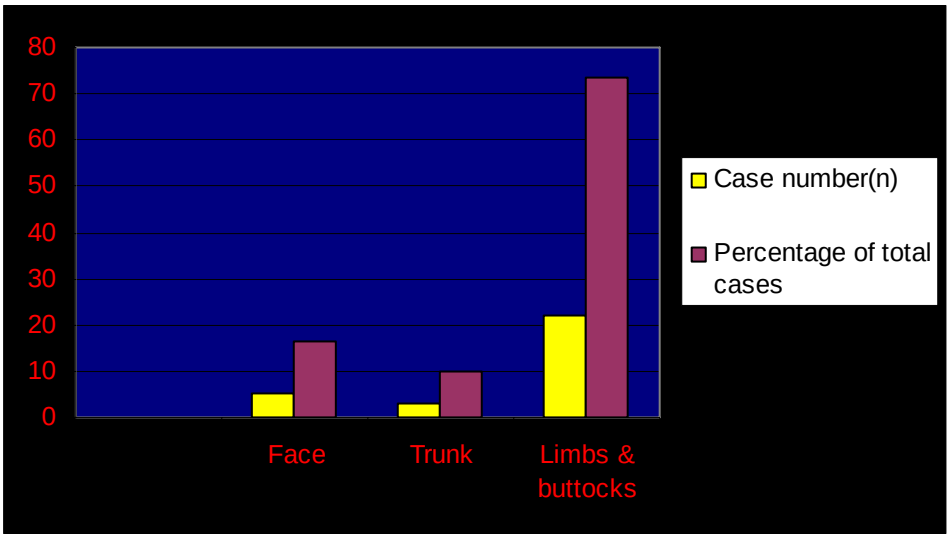
Age group(years)	Case number(n)	Percentage of total cases
Less than 10	1	3.33
11 – 20	6	20
21 - 30	8	26
31 – 40	5	16.66
41 – 50	4	13.33
More than 50	6	20

SEX DISTRIBUTION OF VARIOUS MORPHOLOGICAL TYPES OF CUTANEOUS TB



Clinical types	Male	Female
Warty TB	10	4
Lupus vulgaris	4	5
Scrofuloderma	1	1
Papulonecrotic tuberculid	1	1
Lichen Scrofulosorum	1	-
Erythema nodosum	-	2

DISTRIBUTION OF INVOLVED SITES



Anatomical site	Case number(n) (Total cases – 30)	Percentage of total cases
Face	5	16.6
Trunk	3	10
Limbs & buttocks	22	73.3

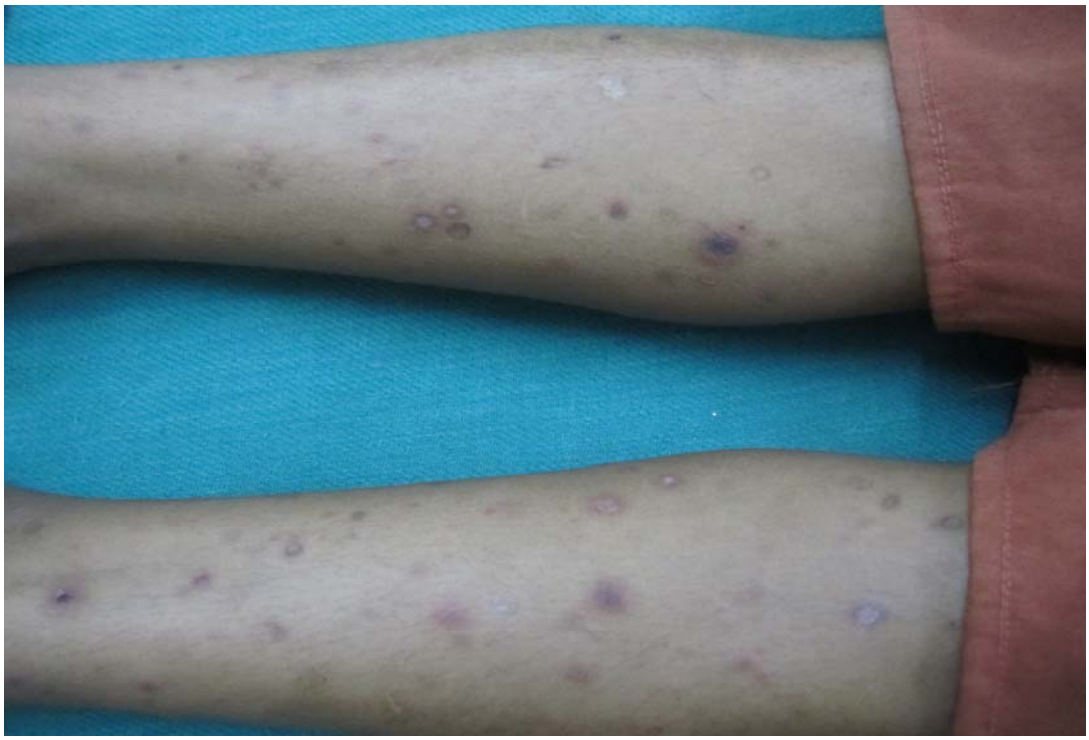
PLAQUE TYPE OFWARTY TUBERCULOSIS

LUPUS VULGARIS

SPOROTRICHOID FORM OF SCROFULODERMA

SCROFULODERMA WITH DACTYLITIS

ERYTHEMATOUS PAPULESWITH CENTRAL NECROSIS AND VARIOLIFORM SCARS IN A CASE OF PAPULONECROTIC TUBERCULID



DISCRETE, SKIN COLOURED ,SCALY PAPULES IN A CASE OF LICHEN SCROFULOSORUM

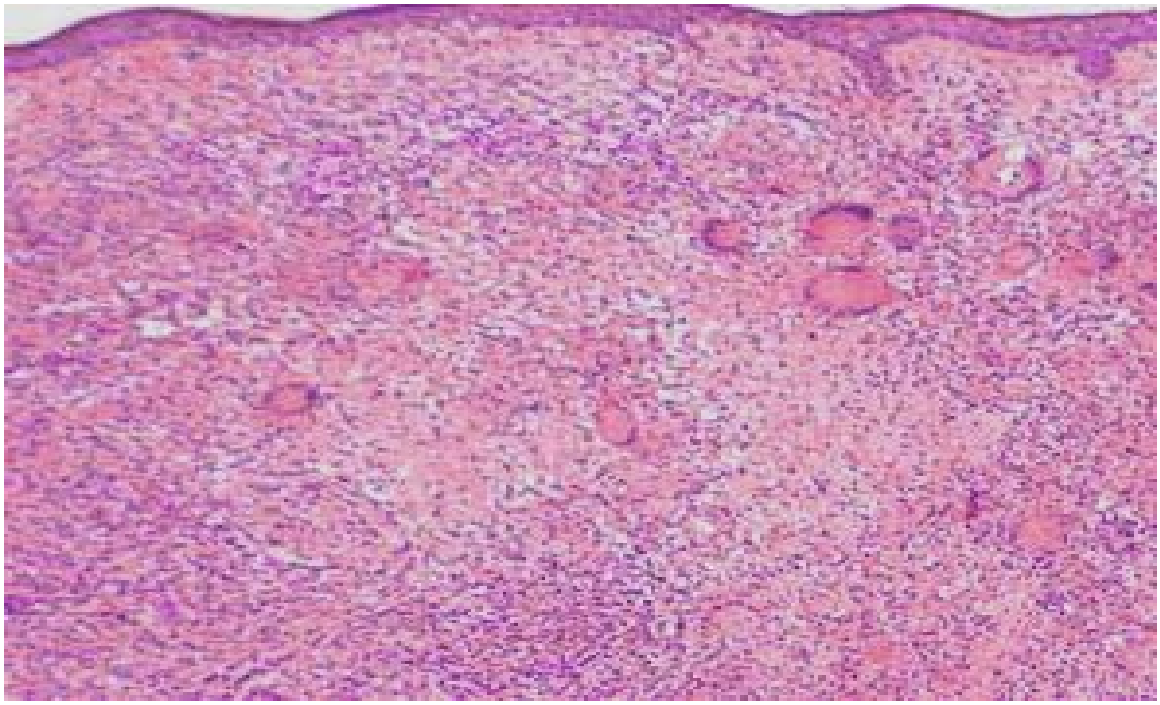
ERYTHEMA NODOSUM

WARTY TUBERCULOSIS

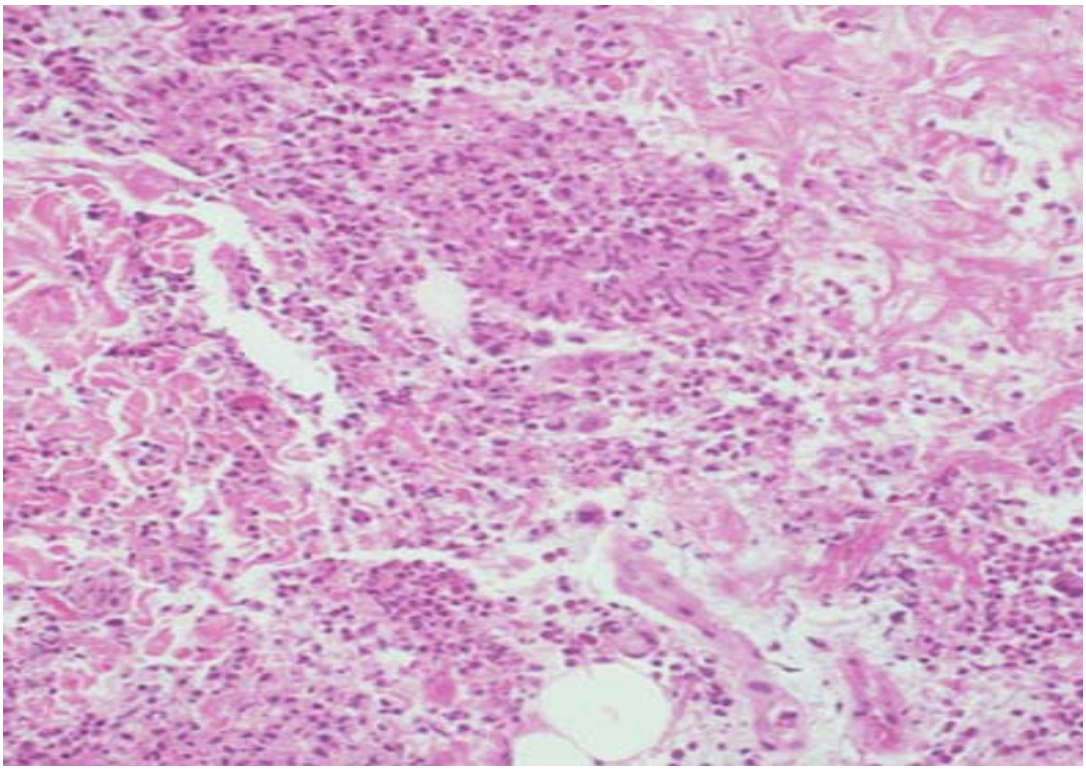
LUPUS VULGARIS

WARTY TUBERCULOSIS WITH TUBERCULOUS LYMPHADENITIS

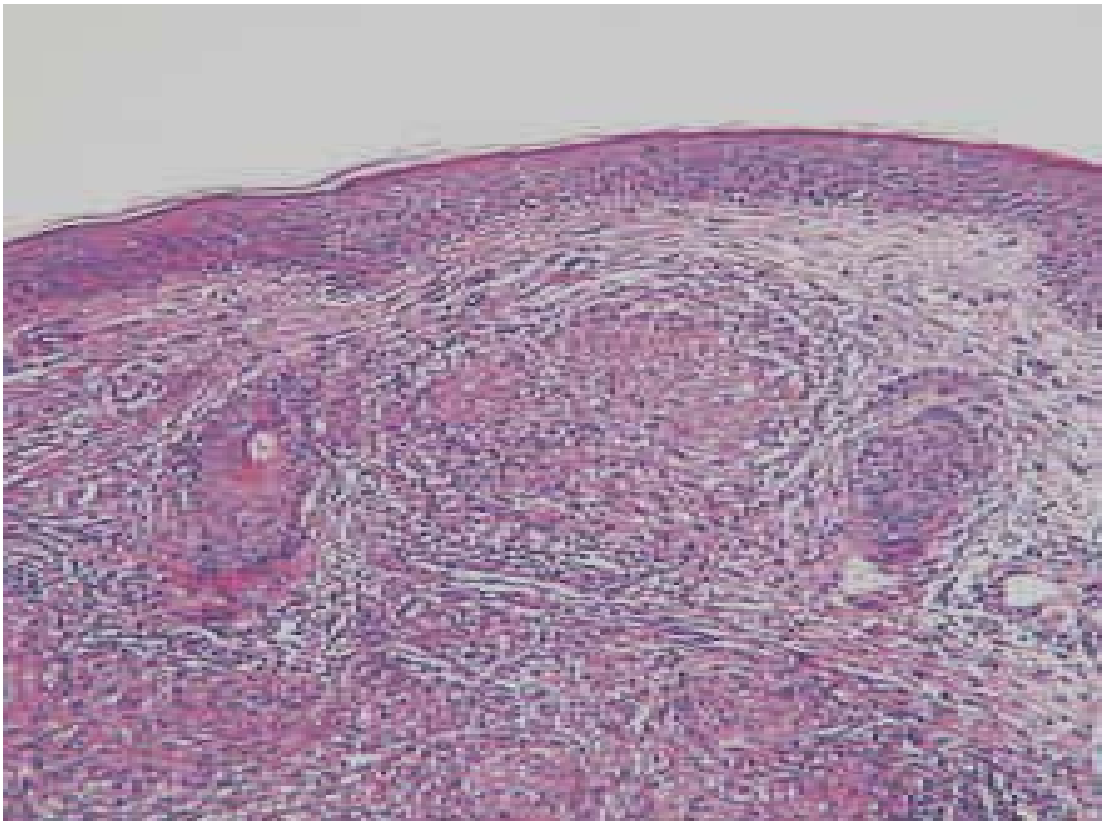
Section showing numerous Langhans giant cells and ill-formed tuberculoid granulomas in upper dermis - Lupus vulgaris



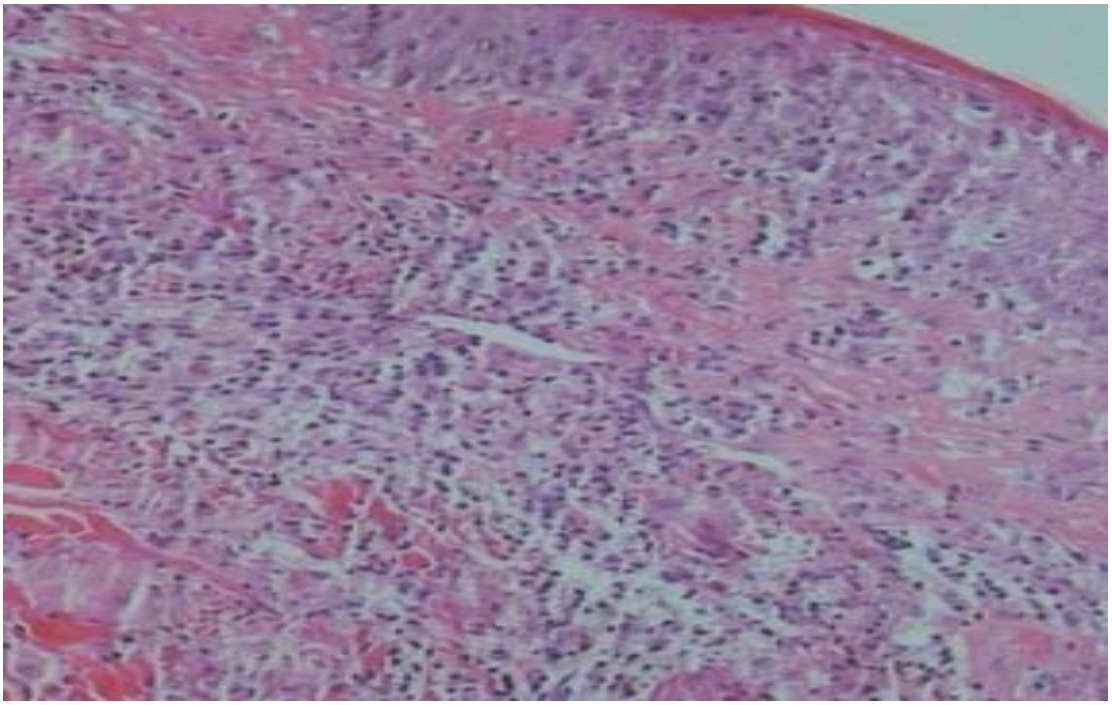
Section showing septal panniculitis – Erythema nodosum



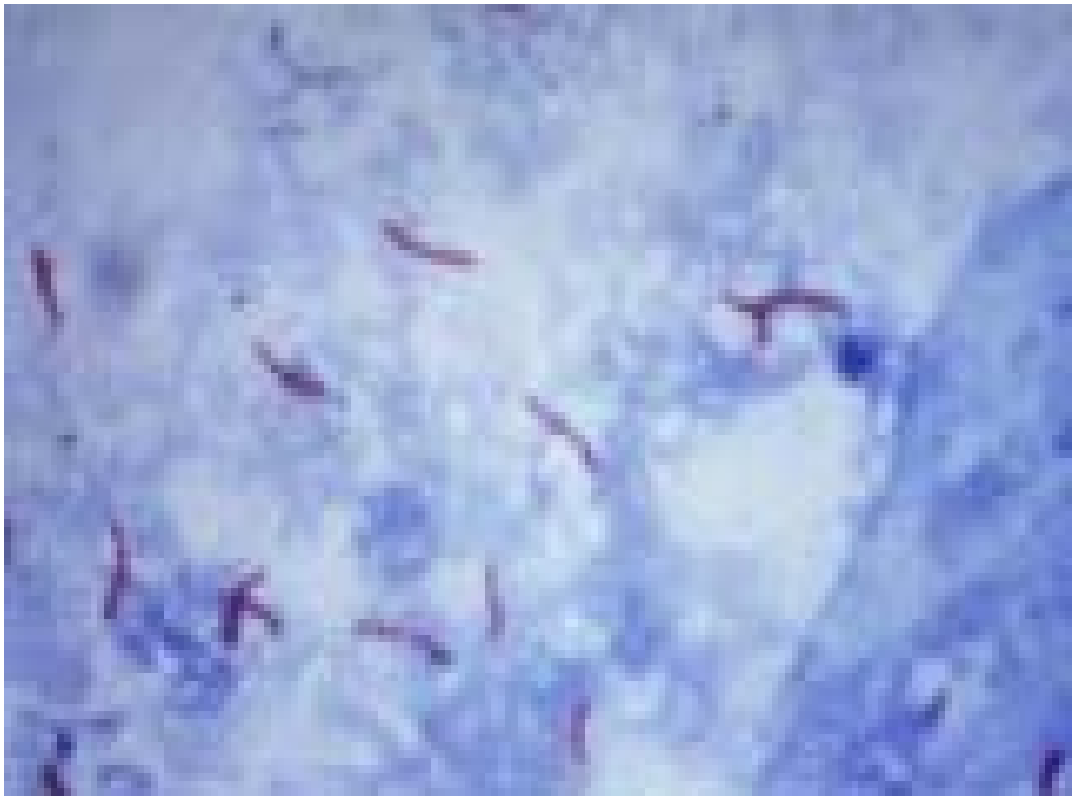
Section showing tuberculoid granulomas in mid dermis – Warty tuberculosis



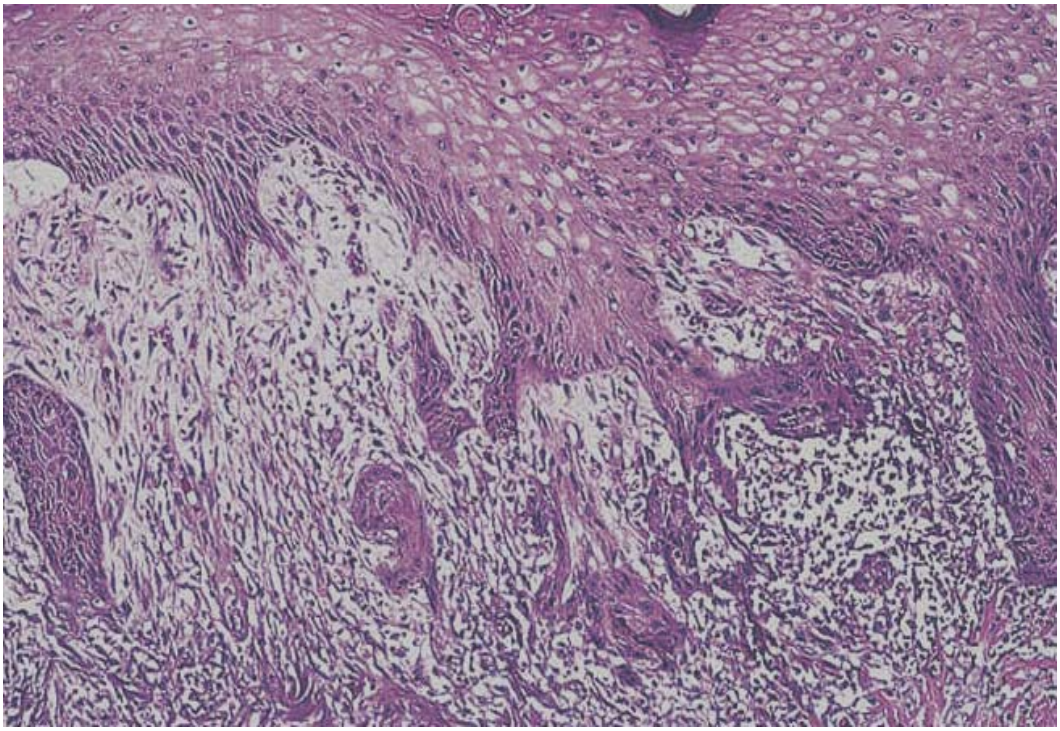
Section showing ill-formed epitheloid cell granuloma - scrofuloderma



Section stained with Ziehl-Neelson stain showing AFB in a case of scrofuloderma



Section showing pseudoepitheliomatous hyperplasia in a case of Warty TB



DISCUSSION

Tuberculosis can involve any organ or tissue of the body including skin. Patients with cutaneous TB present with diverse forms ranging from single, smooth papule to disseminated, eruptive papules, verrucous or vegetative plaques, ulceration, sinus tracts. Acute military TB occurs in patients with severe immunosuppression. Lupus vulgaris and scrofuloderma are seen in patients with less immunosuppression. Warty TB is a localized form, seen in immunocompetant individuals.

In previous studies by Bannerjee[47], the incidence of lupus vulgaris to be 38.29%, warty tuberculosis was 19.14%, scrofuloderma was 14.89%, gumma was 12.76% and these results were consistent with Khan et al[48] , who also found lupus vulgaris as the commonest followed by warty tuberculosis and scrofuloderma. Singh and Kumar et al also found lupus vulgaris as the commonest form. Wong et al [49]found warty tuberculosis as the commonest form(46%), followed by lupus vulgaris (22%)

In our study, which included 30 cases, warty tuberculosis was the commonest form(46.6%), followed by lupus vulgaris(30%). This correlated with the study by Wong et al[49]. Men were most commonly found to be affected than women and the

incidence in males was 56.6% and in females 43.3%. Warty TB was found to be common in males,the incidence being 33.3% and lupus vulgaris was found to be more common in females the incidence being 16.6% is correlated with Singh and kumar et al[50].

Out of 14 cases of warty TB, 78% patients showed classical tuberculoid granulomas in the mid dermis and epidermal changes were present in 70% cases. Patients with lupus vulgaris classic epidermal changes were present in 75% cases and Langhans giant cells could be seen in 82% cases. Amongst the 2 cases of scrofuloderma, 1 case showed ulceration with tuberculoid granulomas and AFB could be demonstrated by special staining and this picture was consistent with that described by Lever[51].

Other than the classical pattern of epitheloid granuloma, Langhans giant cells, caseous necrosis, several other patterns have been described and should be looked for. These patterns include abscess, diffuse infiltration of histiocytes, panniculitis, phlebitis, nonspecific chronic inflammation, naked non necrotic sarcoidal granuloma, rheumatoid like nodules. In our cases panniculitis was present in 2 cases of erythema nodosum. There was nonspecific histopathological picture in one case of scrofuloderma with showed chronic lymphohistiocytic infiltrate and this has been reported by Santa cruz and Strayer in their study[52].

Most common site of involvement was the lower extremity. Wong et al reported that knees and buttocks were the common sites involved in TBVC, similar to the studies by singh. In our study, 21 – 30 years age group was the most commonly affected, which was also noticed in studies by Sathyanarayanan and Wong[53].

There was no association with HIV infection in the cases studied. Past history of pulmonary tuberculosis was present in 3 patients. Chest x-ray findings consistent with tuberculosis were present in 10 cases and raised ESR and Mantoux positivity were present in almost all cases. Most cases belonged to a lower socio economic status , the increased risk probably attributed to over crowding , poor hygiene andmalnutrition.

CONCLUSION

Following were the conclusions derived from this study, which included 30 cases

- Warty tuberculosis was the commonest type followed by lupus vulgaris.
- There was an increased incidence of warty tuberculosis among males and lupus vulgaris among females.
- Majority of the patients belonged to 20-30 years age group.
- Clinicopathological correlation was present in all cases except one case of scrofuloderma.
- Most of the patients belonged to low socioeconomic status, the risk probably due to over crowding, poor hygiene and malnutrition.

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ANNEXURES

PROFORMA

Name Age Sex

Occupation

Address

Percapita income

Complaints

Duration

H/O evening rise of temperature

H/O cough with expectoration

H/O loss of weight and appetite

H/O trauma

Past history - Diabetes/ Hypertension/ Tuberculosis

Family history

Personal history

Treatment history

General examination:

Built

Nourishment

Febrile

Pallor

Icterus

Clubbing

Lymphadenopathy

PR- BP-

CVS

RS

P/A

CNS

Dermatological examination:

Number of lesions

Site

Size

Shape

Surface

Colour

consistency

Nature of lesion

Skin surrounding the lesion

Expression of pus from the lesion on manipulation

Diascopy - presence or absence of apple-jelly nodules

Probe test – probe can or cannot be passed through the lesion

Mucosal involvement

Nails

Hair

MASTER CHART

s.no	Name	Age	Sex	Status	Mantoux	ESR	Chest x-ray	HIV status	H/O TB	Biopsy	AFB stain	Diagnosis
1.	Murali	15	M	Middle	+	15	Normal	Non reactive	-	Consistent with TBVC	-	TBVC
2.	Karthik	25	M	Middle	+	20	Hilar adenitis	Non reactive	-	Consistent with TBVC	-	TBVC
3.	Sarala	42	F	Low	+	15	Normal	Non reactive	-	Consistent with Lupus vulgaris	-	Lupus vulgaris
4.	Ramachandran	28	M	Low	+	25	Normal	Non reactive	-	Consistent with PNT	-	Papulonecrotic tuberculid
5.	Navab khan	26	M	Low	+	15	Normal	Non reactive	-	Consistent with Lupus vulgaris	-	Lupus vulgaris
6.	Hari babu	20	M	Low	+	10	Normal	Non reactive	-	Consistent with TBVC	-	TBVC
7.	Selvi	18	F	Low	-	45	Apical opacity	Non reactive	-	Inconsistent	+	Scrofulodeerma
8.	Janaki raman	36	M	Middle	+	25	Normal	Non reactive	-	Consistent with TBVC	-	TBVC
9.	Kalai priyan	14	M	Low	+	10	Normal	Non reactive	-	Consistent with TBVC	-	TBVC
10.	Kasiammal	54	F	Low	+	15	Apical opacity	Non reactive	+	Septal panniculitis	-	Erythema nodosum
11.	Jothi	55	M	Low	+	45	Pneumonitis	Non reactive	-	Consistent with scrofuloderma	-	Scrofulodeerma
12.	Manohar	11	M	Middle	+	10	Normal	Non reactive	-	Consistent with TBVC	-	TBVC
13.	Saroja	54	F	Middle	+	I5	Normal	Non reactive	-	Consistent with TBVC	-	TBVC
14.	Raja	45	M	Low	+	10	Apical cavity	Non reactive	+	Consistent with Lupus vulgaris	-	Lupus vulgaris
15.	kadaliamma	64	F	Low	+	25	Old healed PT	Non reactive	-	Consistent with PNT	-	Papulonecrotic tuberculid

MASTER CHART

s.no	Name	Age	Sex	Status	Mantoux	ESR	Chest x-ray	HIV status	H/O TB	Biopsy	AFB stain	Diagnosis
16.	Rajesh	28	M	Low	+	20	Normal	Non reactive	-	Consistent with TBVC	-	TBVC
17.	Nagarajan	18	M	Low	+	15	Normal	Non reactive	-	Consistent with Lupus vulgaris	-	Lupus vulgaris
18.	Pradeep	10	M	Low	+	10	Hilar adenitis	Non reactive	-	Tuberculoid granulomas +	-	Lichen scrofulosorum
19.	Vijaya	30	F	Middle	+	10	Apical opacity	Non reactive	-	Consistent with Lupus vulgaris	-	Lupus vulgaris
20.	Velaiyah	5o	M	Low	+	10	Healed PT	Non reactive	+	Consistent with TBVC	-	TBVC
21.	Saraswati	52	F	Low	+	10	Normal	Non reactive	-	Consistent with Lupus vulgaris	-	Lupus vulgaris
22.	Velu	45	M	Low	-	15	Normal	Non reactive	-	Consistent with TBVC	-	TBVC
23.	Devi	28	F	Low	+	5	Normal	Non reactive	-	Consistent with TBVC	-	TBVC
24.	Selvam	56	F	Low	+	35	Hilar adenitis	Non reactive	-	Septal panniculitis	-	Erythema nodosum
25.	Ramesh	22	M	Middle	+	25	Normal	Non reactive	-	Consistent with Lupus vulgaris	-	Lupus vulgaris
26.	Arjunan	36	M	Low	+	15	Normal	Non reactive	-	Consistent with TBVC	-	TBVC
27.	Lakshmi	34	F	Low	+	10	Normal	Non reactive	-	Consistent with Lupus vulgaris	-	Lupus vulgaris
28.	Kannagi	40	F	Low	+	20	Normal	Non reactive	-	Consistent with Lupus vulgaris	-	Lupus vulgaris
29.	Rama laxmi	32	F	Low	+	15	Normal	Non reactive	-	Consistent with Lupus vulgaris	-	Lupus vulgaris
30.	Raju	25	M	Low	+	15	Normal	Non reactive	-	Consistent with Lupus vulgaris	-	Lupus vulgaris

INFORMED CONSENT FORM

I have been fully explained by the doctors about the study and I also give my consent to undergo

the investigations done in this study.

Station: Chennai. Patient's signature

Date: